REMARKS

This amendment is submitted concurrently with a Request for Continued Examination. This amendment addresses the rejections in the Final Office action dated May 21, 2003.

I. Amendments

Typographical errors in the specification are corrected.

A sequence identifier is included for the peptide sequence recited on page 17, line 6.

Claim 1 is amended to remove the term "over-producing" which was inadvertently left in the amended claim in applicants March 4, 2004 amendment.

Claim 25 is amended to correct a typographical error.

No new matter is added by these amendments.

II. Objection to the Specification

The Examiner objected to the specification as being not in compliance with the sequence rules. Reference to a peptide sequence on page 17, line 6 is now identified with a sequence identifier. Also, submitted herewith is a diskette and paper copy of a sequence listing for compliance with the sequence rules.

III. Rejections under 35 U.S.C. §112, second paragraph

Claims 1 and 25 was rejected under 35 U.S.C. §112, second paragraph as being indefinite.

Specifically, claim 1 was rejected on the grounds that the term "overexpression" is relative and renders the claim indefinite. Applicants direct the Examiner to the definition of "overexpression of a cytokine-regulatory factor", *e.g.*, PKR, on page 4, line 31 et seq. In light of the definition provided in the specification, the term is not indefinite and reconsideration is respectfully requested.

With respect to claim 25, the Examiner notes a typographical error in the word "cytokines". Claim 25 is amended to correct this error.

In light of these amendments and comments, withdrawal of the rejection under 35 U.S.C. §112, second paragraph is respectfully requested.

IV. Double Patenting

Claims 1, 2, 10, 25, and 26 were provisionally rejected under the judicially created judicially created doctrine of obviousness-type double patenting at being unpatentable over claims 1-7 and 15-22 of application serial no. 10/105,100.

Applicants respectfully request that this rejection be held in abeyance until allowable subject matter is identified in one of the pending cases.

V. Rejection under 35 U.S.C. §102(b)

Claims 1, 25, and 26 were rejected under 35 U.S.C. §102(b) as being anticipated by Lau (WO 97/08324) in view of Der (*PNAS*, Vol. 92, pp. 8841-8845, 1995). This rejection is respectfully traversed for the following reason.

The present invention relates to a composition produced by a specified process. The process includes the step of "culturing a human cell line (i) capable of producing cytokines, and (ii) transformed with a PKR gene and a gene that expresses a protein effective to inhibit apoptosis in the cell line, in a culture medium effective to cause overexpression of PKR and the anti-apoptotic protein in the mammalian cell line."

The composition and process described by Lau does not include culturing cells that express two genes – a PKR gene and an apoptitic protein. The teaching in Lau is limited to a showing of cells expressiing a PKR gene.

Because of this difference, there is no basis for asserting that the claimed product appears to be the same or similar to that of Lau. Withdrawal of the rejection is respectfully requested.

VI. Rejections under 35 U.S.C. §103

Claims 1, 2, 10, 25 and 26 were rejected under 35 U.S.C. §103(a) as being obvious over Kurimoto (U.S. Pat. No. 5,362,490) in view of Shimizu (U.S. Pat No. 4,474,754).

This rejection is respectfully traversed in view of the foregoing claim amendments and following remarks.

A. The Invention

The present invention, as embodied in claim 1, is directed to a composition containing a mixture of human cytokines produced by (a) culturing a human cell line (i) capable of producing cytokines, and (ii) transformed with a PKR gene and a gene that expresses a protein effective to inhibit apoptosis in the cell line, in a culture medium effective to cause overproduction overexpression of PKR and the anti-apoptotic protein in said mammalian cell line; (b) treating the PKR-overproducing cell line to induce cytokine production; and (c) isolating cytokines produced by said cultured, PKR-overproducing cell line and secreted into culture medium.

Producing the mixture of cytokines in the manner described and claimed provides two important advantages:

(1) human cytokine producing cells are employed that have the ability to produce the desired, complex mixture of cytokines for use therapeutically; and

(2) the mixture is produced at high levels at a stoichiometric ratio that the body recognizes as a natural mixture of cytokines.

B. The Cited Art

Kurimoto *et al.* is directed to overexpressing a novel human interferon gamma. The reference is not concerned with the problem addressed by the present invention, nor does it suggest the applicants' solution. In particular, the reference does not show or suggest producing a cytokine mixture at a high level that is stoichiometrically similar to that produced physiologically, nor does the reference show or suggest producing the mixture from a single cell line that has been selected for its ability to produce the desired combination.

Shimizu teaches the production of human interferon antibodies. The reference is not concerned with the problem addressed by the present invention, nor does the reference suggest the applicants' solution, or the advantages thereof, for the same reasons applied to Kurimoto.

C. Legal Standard of Obviousness

In determining whether an invention is nonobvious, the PTO has the burden of establishing a case of *prima facie* obviousness. A proper analysis under 35 U.S.C. §103 requires consideration of whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process and whether the prior art would have also revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success. Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure. See MPEP §2142, citing *In re Vaeck,* 20 USPQ2d 1438, Fed. Cir. 1991.

Thus, for a combination of references to render a claimed invention obvious under 35 U.S.C §103, that combination must provide not only a suggestion of the present invention, but also a reasonable expectation of success in reaching that invention. Under these standards, and as discussed below, the Examiner has not made a *prima facie* case of obviousness. In order for the prior art to provided motivation for combining references along the lines of the invention, the prior art must recognize the advantages to be gained by such combination. As noted above, none of the references cited is concerned with the problem of achieving high levels of production of mixtures of cytokines in selected cells at a ratio that the body recognizes as a natural mixture, nor recognizes or even suggests the possibility of addressing the problem successfully by the overexpression of PKR or an anti-apoptotic protein.

In the absence of such a suggestion, and failing to recognize the problem addressed by the present invention, and its solution, the prior art cannot be said to provide a suggestion or motivation for the claimed invention.

Dependent claims 2, 10, 25 and 26 incorporate all the subject matter of claim 1 and add additional subject matter, which makes them *a fortiori* and independently patentable over Kurimoto and Shimizu.

In view of the foregoing, the applicants submit that none of the above references, alone or in combination, renders the pending claims obvious. Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §103.

VII. Conclusion

In view of the foregoing, the applicant submits that the claims pending in the application comply with the requirements of 35 U.S.C. §112 and patentably define over the prior art. A Notice of Allowance is therefore respectfully requested.

If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 838-4402.

Respectfully submitted,

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